From the
INTERNATIONAL SEARCHING AUTHORITY

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# PCT

## WRITTEN OPINION OF THE INTERNATIONAL SEARCHING AUTHORITY
(PCT Rule 43*bis*.1)

Date of mailing
*(day/month/year)* see form PCT/ISA/210 (second sheet)

Applicant's or agent's file reference
see form PCT/ISA/220

**FOR FURTHER ACTION**
See paragraph 2 below

| International application No. | International filing date *(day/month/year)* | Priority date *(day/month/year)* |
|---|---|---|
| PCT/EP2004/052725 | 29.10.2004 | 31.10.2003 |

International Patent Classification (IPC) or both national classification and IPC
A61K31/519, A61K31/195

Applicant
ALTANA PHARMA AG

1. This opinion contains indications relating to the following items:

- ☒ Box No. I Basis of the opinion
- ☐ Box No. II Priority
- ☐ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
- ☐ Box No. IV Lack of unity of invention
- ☒ Box No. V Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
- ☐ Box No. VI Certain documents cited
- ☐ Box No. VII Certain defects in the international application
- ☐ Box No. VIII Certain observations on the international application

2. **FURTHER ACTION**

If a demand for international preliminary examination is made, this opinion will usually be considered to be a written opinion of the International Preliminary Examining Authority ("IPEA"). However, this does not apply where the applicant chooses an Authority other than this one to be the IPEA and the chosen IPEA has notifed the International Bureau under Rule 66.1*bis*(b) that written opinions of this International Searching Authority will not be so considered.

If this opinion is, as provided above, considered to be a written opinion of the IPEA, the applicant is invited to submit to the IPEA a written reply together, where appropriate, with amendments, before the expiration of three months from the date of mailing of Form PCT/ISA/220 or before the expiration of 22 months from the priority date, whichever expires later.

For further options, see Form PCT/ISA/220.

3. For further details, see notes to Form PCT/ISA/220.

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**Box No. I Basis of the opinion**

1. With regard to the **language**, this opinion has been established on the basis of the international application in the language in which it was filed, unless otherwise indicated under this item.

   ☐ This opinion has been established on the basis of a translation from the original language into the following language , which is the language of a translation furnished for the purposes of international search (under Rules 12.3 and 23.1(b)).

2. With regard to any **nucleotide and/or amino acid sequence** disclosed in the international application and necessary to the claimed invention, this opinion has been established on the basis of:

   a. type of material:

   ☐ a sequence listing

   ☐ table(s) related to the sequence listing

   b. format of material:

   ☐ in written format

   ☐ in computer readable form

   c. time of filing/furnishing:

   ☐ contained in the international application as filed.

   ☐ filed together with the international application in computer readable form.

   ☐ furnished subsequently to this Authority for the purposes of search.

3. ☐ In addition, in the case that more than one version or copy of a sequence listing and/or table relating thereto has been filed or furnished, the required statements that the information in the subsequent or additional copies is identical to that in the application as filed or does not go beyond the application as filed, as appropriate, were furnished.

4. Additional comments:

**Box No. V Reasoned statement under Rule 43*bis*.1(a)(i) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement**

1. Statement

| | | | |
|---|---|---|---|
| Novelty (N) | Yes: | Claims | |
| | No: | Claims | 1-2,10,23 |
| Inventive step (IS) | Yes: | Claims | |
| | No: | Claims | 1-4,6,8,10 |
| Industrial applicability (IA) | Yes: | Claims | 1-23 (cf.text) |
| | No: | Claims | |

2. Citations and explanations

**see separate sheet**

D1: WO 01/56551
D2: EP-A-0 908 182 (cited in the application)
D3: WO 96/02245

1. The application discloses, inter alia, the use of a combination of tetrahydrobiopterin (BH4) and arginine (derivatives) for the treatment of respiratory diseases.
   A synergistic effect appears to be present for this combination (example 6/page 14, last paragraph, fig. 3a).

2. Document D1 discloses the use of BH4 (precursors) and cGMP analogues for the treatment of resiratory diseases such as pneumonia and asthma.

   Document D2 discloses the use of BH4 (derivatives) for the treatment of diseases associated with dysfunction of NOS (nitric oxide synthase), e.g. hypertension and renal disorders.

   Document D3 discloses the use of arginine derivatives such as L-NMMA which are NOS inhibitors for the treatment of respiratory diseases such as cystic fibrosis and chronic bronchitis.

3. Claims 1-2 and 10 are not novel and claims vis-a-vis document D1. Claims 3-4, 6, and 8 are not inventive in view of this document.

   Claim 10 is not novel having regard to document D2.

   Due to the word "or" in line 1 claim 23 is not novel in view of document D1, D2 or D3.

4. For the assessment of the present claims 6-7, 15, 21 on the question whether they are industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment

and the use of such a compound for the manufacture of a medicament for a new medical treatment.